# Sensorimotor Mapping of the Human Cerebellum: fMRI Evidence of Somatotopic Organization

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Abstract: Functional magnetic resonance imaging (fMRI) was employed to determine areas of activation in the cerebellar cortex in 46 human subjects during a series of motor tasks. To reduce the variance due to differences in individual anatomy, a specific transformational procedure for the cerebellum was introduced. The activation areas for movements of lips, tongue, hands, and feet were determined and found to be sharply confined to lobules and sublobules and their sagittal zones in the rostral and caudal spino-cerebellar cortex. There was a clear symmetry mirroring at the midline. The activation mapped as two distinct homunculoid representations. One, a more extended representation, was located upside down in the superior cerebellum, and a second one, doubled and smaller, in the inferior cerebellum. The two representations were remarkably similar to those proposed by Snider and Eldred [1951] five decades ago. In the upper representation, an intralimb somatotopy for the right elbow, wrist, and fingers was revealed. The maps seem to confirm earlier electrophysiological findings of sagittal zones in animals. They differ, however, from micromapping reports on fractured somatotopic maps in the cerebellar cortex of mammals. We assume that the representations that we observed are not solely the result of spatial integration of hemodynamic events underlying the fMRI method and may reflect integration of afferent peripheral and central information in the cerebellar cortex. Hum. Brain Mapping 13:55–73, 2001. © 2001 Wiley-Liss, Inc.

Key words: functional magnetic resonance imaging (fMRI); cerebellum; somatotopy; voluntary movement; brain mapping

#### INTRODUCTION

The cerebellum plays an important part in movement control. In particular, the spino- and vestibulocerebellum have been associated with the integration of sensory and motor information. In 1945, Hampson et al. first reported somatotopic representations of mo-

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tor responses in the cerebellum of the cat and the dog. These findings were extended and summarized by Snider and Eldred [1951] on the basis of proprioceptive, tactile, auditory, and visual stimulation, as well as electric stimulation of the telencephalon in cats and monkeys. Two well-shaped animalculi were described; one located upside down in the superior and a second, duplicated one, in the inferior cerebellar aspect. Consequently, similar maps have been hypothesized in humans.

In the human cerebellum, however, the distribution of functions and to what extent they serve the sensorimotor system is still uncertain [Schmahmann, 1997]. While somatotopic representation in the telencepha-

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lon of sensorimotor areas-with separate areas for various parts-has stood the tests of time [Jackson, 1895; Penfield and Boldrey, 1937; Woolsey et al., 1952], a precise somatotopic arrangement in the human cerebellum has not been established. According to the existing topodiagnostic scheme, in humans, motor deficits are commonly due to lesions in the lateral, intermediate, and vermal zones. In general, this is consistent with the findings of Snider and Eldred [1951] inasmuch as (i) lateral cerebellar damage predominantly results in a delay of movement initiation and in a decomposition of multijoint movementsinvariably more pronounced in the arm, (ii) paramedian lesions often cause dysarthria, and (iii) lesions to the vermis produce ataxia of stance and gait [Dichgans and Diener, 1985]. Furthermore, a detailed functional analysis of the human cerebellum has been hampered by the anatomical characteristics of the posterior fossa, in which it remained inaccessible for most of the commonly applied mapping techniques.

Only after the advent of positron emission tomography (PET) and fMRI did it become possible to detect cerebellar activation during natural movements in humans. A survey of these functional studies is summarized in Table I. In general, the studies confirmed the findings of Snider and Eldred [1951] with regard to the anterior-posterior body representation but failed to depict a medio-lateral somatotopic arrangement. Additionally, however, multifocal, parasagittally, and transversely oriented activation patterns were observed. These showed considerable interindividual variation. Ipsilaterality of movement and activation as well as neocerebellar activation was often, but inconsistently, found [Fox et al., 1985; Ellerman et al., 1994; Britsch et al., 1996; Nitschke et al., 1996; Sakai et al., 1998]. Because only two fMRI studies contained group statistics [Desmond et al., 1997; Allen et al., 1997] and only four covered the whole cerebellum [Ellerman et al., 1994; Britsch et al., 1996; Sakai et al., 1998], a refined, functional-topographical description of cerebellar activities during various movements of different body parts remains uncharted.

Functional studies with PET and fMRI of the cerebrum are normally subjected to group statistics performed within a normalized reference space to accomplish a probabilistic mapping of brain activity within that space [Talairach and Tournoux, 1988]. The Talairach system, however does not include the cerebellum. Probabilistic mapping of neuronal activity in cerebellar areas has thus only very recently been initiated [Doyon et al., 1999]. Such mapping requires a special adaptation of the transformational procedure. We have thus introduced such a cerebellar-specific transformation procedure, based on physical distances, to examine the consistency and relationships of fMRI activation sites in the cerebellum among humans as they performed a series of motor tasks. In our study, various natural movements of the face (tongue, lips), the arm (elbow, wrist, hand, fingers), and the foot were examined by the use of group statistics to assess the anatomical-functional relations in greater detail.

### MATERIALS AND METHODS

### Subjects

Forty-six subjects were recruited from the academic environment of the University of Tübingen. They suffered from no physical, neurological, or psychiatric disorders. The study was conducted in accordance with the Declaration of Helsinki and with the approval of the local committee on medical ethics. All subjects gave full informed consent for participation in the study. All were right-handed (30 male, 16 female, 18–56 years, mean 35.6 years). Handedness was qualitatively assessed by means of the Edinburgh Handedness Inventory [Oldfield, 1971]. Anatomical magnetic resonance imaging (MRI) data from 20 other subjects (11 male, 9 female, 18–41 years, mean 32.4 years) served as a reference for cerebellar normalization.

### **Experimental tasks**

The subjects performed the following movements at a frequency of one movement per second (acoustically indicated by a metronome): (a) opening/closing the right or left fist (n = 10); (b) pursing the lips (n = 10); (c) moving the tongue vertically (n = 9); (d) flexing/ extending the right or left foot (n = 5); (e) flexing/ extending the right hand (n = 10); (f) flexing/extending the right forearm (n = 9); and (g–j) individual tapping of the right fingers I, II, III and V (n = 10). Subjects' eyes were closed to avoid additional oculomotor activation. All participants were trained prior the examination period and each action was performed four times for 1 min each followed by a rest period of 1 min.

### **MRI** data acquisition

All data were acquired with a 1.5 Tesla whole-body system using multislice imaging of the whole brain. Anatomy was obtained by 3D imaging with a FLASH sequence (128 slices, 1.5-mm thickness, 1-mm<sup>2</sup> in-plane resolution) with a repetition time (TR) of 20 ms and an echo time (TE) of 5 ms. fMRI was performed with an

First author	Year	Imaging method	Resolution (mm)	Slices (#)	Body part	Applied paradigm	Freq. (Hz)	Pacing	Location and pattern
xot	1985	PET	12  imes 12  imes 14		Hand Hand	Tactile stimulation Bilateral, opening and closing, brisk	$^{130}_{\sim 2}$	Vibratory Self-paced	Ipsilateral, anterior lobe Bilateral, anterior lobe
Colebatch	1991	PET	$8.5 \times 8.5 \times 7$		Digitus II	Abduction and adduction of index	1.5	Metronome	
					Shoulder	unger Vertical flexing of shoulder	1.5	Metronome	Superior vermis
					Fingers Hand	Opposition of thumb to each finger Fist making	1.5 1.5	Metronome Metronome	
Grafton	1993	PET	$16 \times 16 \times 16$		Digitus II	Moving second metacarpophalangeal			Ipsilateral, anterior lobe
					Thumb	Moving first metacarpophalangeal			Ipsilateral, anterior lobe
					W/wist	Joint Hand hold lichtly in a fiet			Trailatoral antonior Joho
					Elbow	Wrist passively flexed			Ipsuateral, atterior lobe Ipsilateral, anterior lobe
					Shoulder	Hand placed against opposite			Ipsilateral, anterior lobe
Illerman	1994	fMRI	$11 \times 1.25 \times 1.25$	Ŋ	Wrist	Flexion/extension of the supinated forearm	1	Visual-paced	Ipsilateral, anterior lobe, fragmented areas, Parasagittal, intermediate + lateral bands, dentato miniens
lament	1996	fMRI	$11 \times 1.25 \times 1.25$	4	Arm	Step-tracking task, hold and move a joystick	$\sim 0.2$	Visual-paced	Ipsilateral vermal, paravermal and later zones
ßritsch	1996	fMRI	$5 \times 3 \times 3$	27	Hand	Opening and closing the right/left hand	<u>~</u>	Self-paced	Conuguous acuvanon in LIVILA CF. I Ipsilateral, superior posterior hemisphere, Inferior intermediate, medio-laterally oriented
					Foot	Flexing and extending the right/left foot	~	Self-paced	Ipsilateral, anterior hemisphere Inferior intermediate hemisphere
Vitschke	1996	fMRI	$4 \times 0.78 \times 0.78$	Ю	Wrist	Extend and flex right hand	~2	Self-paced	Ipsilateral, intermediate HIV-V, medio- lateral
					Foot	Extend and flex right foot	$^{\sim}2$	Self-paced	Ipsilateral, HII-III, medio-lateral bands
					Tongue	Horizontal movements	rapidly	Self-paced	<b>Unilateral</b> , HVI, medio-lateral bands
Allen Desmond	1997 1997	fMRI fMRI	$6 \times 5.5 \times 5.5$ $6 \times 2 \times 2$	e 9	Hand Fingers	Movement of the right hand Right thumb to each finger, Read	rapidly	Self-paced	Ipsilateral, HIV-HV, I–V Bilateral, mainly ipsilateral, HIV/V, IV,
					Tongue	subvocally letters			V, HVI, HVIII, HVII, HVIIA, cr. I
ueptner	1997	$\operatorname{PET}$	10  imes 10  imes 6	4	Elbow	Passive elbow flexion with elbow	1	Metronome	Bilateral, mainly ipsilateral, HVI-IX, VI-
						tixed Active elbow flexion and extension	1	Metronome	LX, nuclet Bilateral, mainly ipsilateral, HVI-IX, VI- IX muclei
akai	1998	fMRI	7  imes 1.7  imes 1.7	10	Fingers	Tapping right index finger against thumb	ю	Metronome	Ipsilateral HIV-V, oblique bands
							random		HVIIA

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echo planar imaging sequence [Klose et al., 1999] (27 slices, TE 46 ms, slice thickness 4 mm, in-plane resolution 3 mm<sup>2</sup>, scan time 8 sec), which was repeated 48 times (interscan interval, 10 sec) with six measurements alternating between rest and activation four times.

### **Cerebellar transformation**

A specific linear transformational procedure adapted for the cerebellum was developed in analogy to the spatial normalization procedure for the cerebrum described by Talairach and Tournoux [1988] (Fig. 1). First, seven major anatomical landmarks of the cerebellum were determined in the anatomical 3D data sets of a group of 20 volunteers. These landmarks were: rh = lateral border of the right hemisphere; lh = lateral border of the left hemisphere; ap = anterior pons; dh = dorsalhemisphere; rv = rostral vermis; cv = caudal vermis; ch = caudal hemisphere. Second, by defining three orthogonal planes centered at the floor of the fourth ventricle, the mean values of these landmarks were then used to adjust the individual landmarks of each subject to the determined norm value by linear expansion or compression along these three axes.

The resulting cerebellar template of the transformed and averaged brains served as a 3D-reference space to house the averaged cerebellar anatomy as well as the derived activation maps. For the latter, the same transformation and averaging was performed after individual determination of the activation with identical thresholds (see Image analysis below) and displayed as maximum intensity projections (MIP) maps within the cerebellar template.

### Image analysis

First, a two-dimensional rigid body movement correction was applied to all functional data sets. Activation maps were than determined by correlating a boxcar function of the various motor activities with the time course of the signal intensity [Bandettini et al., 1993]. To correct for the temporal delay of the fMRI signal, the first image of each rest and activation block within the series was discarded. The correlation data were reinterpolated to 1 mm<sup>3</sup>, transformed in the same manner as described above for the anatomical data, and averaged after application of a Gaussian spatial filter ( $\sigma = 2 \text{ mm}$ ). Movement correction, correlation, transformation, and averaging were performed using the AFNI program package [Cox, 1996]. The activation display was achieved by an MIP with uncorrected *P*-values of P < 0.01 and 0.05. The cluster volumes, position of the local maxima, and anatomical location were also determined. For surface display, a transformed cerebellum of a single subject was rendered and the averaged activation volumes were superimposed using the CURRY program package (Neuro Scan, Inc., Sterling, VA).

### RESULTS

The anatomical nomenclature of the cerebellum used here refers to the classification of Larsell and Jansen [1971]. Thus, the cranio-caudal course of the cerebellar anatomy is divided into 10 lobuli (vermis: I-X, hemisphere: HI-X). These are subdivided into up to six lamellae (a–f) (Fig. 1). Although no macroanatomical features subdivide the medio-lateral extent of the cerebellar hemisphere, we have subdivided the medio-lateral course in a vermal, paravermal, intermediate, and lateral compartment in accordance with functional studies [Dow and Andersen, 1942; Voogd, 1967; Jansen, 1969].

### Anatomy

The resulting cerebellar template with its center at the floor of the fourth ventricle (Fig. 1) enabled identification of major fissures and lobules in the sagittal, axial, and coronal planes even after normalization and averaging over 20 individuals. Labeling was most reliable in the anterior cerebellum and in lobuli VI/HVI and VIIA/HVIIA. Such labeling, however, was hardly possible in HVIIB-HIX.

### Individual activation

There was considerable individual variation of the activation volumes (AVs) and the maximal correlation coefficient (MC) with respect to location, extent, and the level of the overall BOLD response among individuals. As an example, the activation maps obtained for hand and lip movements are given in Figure 2 for all 10 subjects. The MC ranged from 0.24 to 0.49, with a mean value of 0.37 for all conditions and all subjects. AV and MC during right and left fist-making (all subjects) were located ipsilateral in the anterior lobe, in intermediate HV, and in vermal V. In the HV region, the individual hand AV varied between 10-25 mm in the medio-lateral, 10-20 mm in the ventrodorsal, and 5-15 mm in the cranio-caudal direction. Additional activation during hand movement was found ipsilateral in HVIII, approximately 15 mm medio-lateral, 10-20 mm ventro-dorsal, and -20 mm cranio-caudal from the center in six subjects. During lip movement, AVs occurred most often bilaterally posterior to the hand area, intermediate in HVI. Lat-



#### Figure I.

Linear transformation of the cerebellum. Upper row: Three perpendicular planes (midsagittal x-plane, y-plane along the floor of the fourth ventricle, z-plane through the apex of the fourth ventricle) centered at the dorsal pons with definition of seven anatomical landmarks (rh = right hemisphere; lh = left hemisphere; rv = rostral vermis; cv = caudal vermis; ch = caudal hemisphere; dh = dorsal hemisphere; ap = anterior pons) used for transformation. Mean values (n = 20) for determined landmarks are given in lower right table. Middle row and lower left: Cerebellar template after linear transformation and averaging with examples of coronal, sagittal, and axial sections, scaled in mm. Long white lines: position of the corresponding slices. Assignments: Roman numbers = lobules; a, b, c, d, e, f =lamellae, according to Larsell and Jansen [1971]; f.h. = fissura horizontalis; f.p. = fissura prima; f.pp. = fissura praepyramidalis; f.s.p. = fissura superior posterior.



#### Figure 2.

Individual activation maps of 10 subjects during repetitive movement of the right hand (red), left hand (green), and lips (blue) (P < 0.05) in coronal and axial projections. The axes scaled in mm. The color intensity scales the correlation coefficient from threshold to

maximum. The individual correlation maxima are given in the upper left of the axial projections for the right hand, left hand, and lips. Assignments: R = right; L = left.

eral, neocerebellar AVs, mostly in HVII, were found for all movements. Multiple, disseminated smaller activation spots occurred during one of the movements in all subjects except one. Within the vermis, the disseminated areas of activation were mostly aligned in sagittally oriented bands, and within the hemisphere; the larger AVs were medio-laterally oriented.

#### **Group results**

Two different threshold levels were chosen for the evaluation of group data (P < 0.01 and 0.05). This resulted in several AVs, the locations of which and the extensions as well as the MCs are presented, with their coordinates, in Tables II and III. To demonstrate the influence of different threshold levels on the AVs for hand, lip, and tongue, the results are shown at both levels in Figure 3.

#### Tongue

cated bilaterally in HVI (left: 2,281 mm<sup>3</sup>; right: 1,687 mm<sup>3</sup>). Rostrally, their medial aspect crossed the primary fissure into HVd–f. Caudally, they respected the fissure intralobularis HVI. The medial borders ran almost perpendicular to the course of the foliae, 7 mm on the right and 11 mm on the left of the midline. The lateral borders of both AVs were located  $\approx 25$  mm apart from the midline. A third AV (844 mm<sup>3</sup>) was situated in left lobulus VI. A fourth AV (823 mm<sup>3</sup>) resided midsagittally in the dorsal medulla. At the lower correlation level (*P* < 0.05), the AVs expanded and a new small AV evolved in right HVIII.

### Lips

Bilateral AVs (Figs. 3, 4) were found in HVIA (left: 544 mm<sup>3</sup>; right: 625 mm<sup>3</sup>). The medial borders of both AVs ran almost perpendicular to the course of the foliae (10 mm lateral to the midline on the right and 15 mm on the left), so that the paravermal hemisphere was spared. The lateral extension did not reach the lateral part of the hemispheres. The AVs were delimited rostrally by the primary fissure. Caudally, they

Body part	Left cerebellum						Right cerebellum						Body	
	AV	mm <sup>3</sup>	MC	х	у	z	Lobule	AV	mm <sup>3</sup>	MC	x	у	z	part
Tongue	1	2,281	0.27	-18	26	3	HVI	2	1,687	0.21	16	22	4	Tongue
										0.21	14	23	6	
										0.18	16	31	4	
	3	844	0.18	-1	35	10	VI			0.15	1	30	15	
							brain stem	4	823	0.17	0	$^{-2}$	-17	
Lips	1	544	0.16	-14	25	5	HVI	2	625	0.16	20	24	6	Lips
Left hand	1	3,735	0.29	-14	13	9	HV	1	3,631	0.21	14	12	8	Right hand
			0.17	$^{-2}$	26	6	V			0.21	4	26	7	0
							V			0.17	5	24	15	
							HV			0.12	17	23	7	
	2	383	0.18	-15	17	-16	HVIII	2	612	0.18	12	17	-20	
Left foot	1	114	0.18	10	1	16	HIV	1	138	0.20	12	2	8	Right foot
										0.18	18	-3	9	0
							HIX	2	37	0.18	7	8	-28	

<b>TABLE II.</b> Localization	for tongue,	lips, hands,	and foot in the	e cerebellar space

Activation volumes (AV's) in mm<sup>3</sup>, their maximal correlation coefficients (MC) and local coordinates (x, y, z) for movements of face, arms and feet at uncorrected P < 0.01 in the left and right cerebellum with designation of lobules. Tongue and lips show a bilateral, symmetrical activation. Note that left and right hand as well as lips and tongue possess a high degree of left to right symmetry in the upper cerebellum.

respected the fissura intralobularis HVI. At the lower correlation level (P < 0.05), the bilateral symmetry as well as the rostral, caudal, and especially the medio-sagittal boundary were mainly preserved, but laterally the areas expanded so that they filled the lateral aspect of the lobulus simplex. A new AV emerged in the vermis in VI and in the left lobulus HVIII.

### Right hand

Two large AVs emerged ipsilaterally (Fig. 3–4). The upper AV (3,631 mm<sup>3</sup>) was formed by two overlap-

ping clusters in VB and HVB. The first cluster filled Vb–f, strictly respected the cerebellar midline as the medial and the primary fissure as the caudal border, and extended only slightly into the hemisphere. This cluster was connected by a thin band in HVb–c with the second cluster, which was located within HVb–f. The second cluster extended in its lateral aspect from HVf into HVId across the primary fissure. The rostral border was formed by the fissura intraculminaris II. The medial and lateral borders ran almost perpendicular to the course of the foliae, 15 and 30 mm apart from the midline, thus sparing the paravermal and

				and migers i		iai space	
Body part	AV	mm <sup>3</sup>	МС	х	У	Z	Lobulus
Right elbow	1	717	0.18	5	31	7	V
0	2	24	0.13	20	6	8	HV
Right wrist	1	2,799	0.20	19	10	8	HV
0			0.19	7	26	8	V
	2	322	0.15	10	18	-19	HVIII
Right thumb	1	2,117	0.19	14	16	9	HV/V
0	2	155	0.14	10	19	-18	HVIII
Right digit II	1	582	0.15	19	15	5	HV
0 0	2	10	0.12	3	27	5	V
Right digit III	1	24	0.12	17	16	7	HV
Right digit V	1	128	0.14	22	12	5	HV

TABLE III. Localization of right elbow, wrist, and fingers in the cerebellar space

Activation volumes (AV's) in mm<sup>3</sup>, their maximal correlation coefficients (MC) and local coordinates (x, y, z) for intralimb movements of the right arm at uncorrected P < 0.01 in the left and right cerebellum with designation of lobules.







#### Figure 4.

Group activation displayed on individual cerebellar template for movements of the hands (right = red; left = green), the lips (blue), and the feet (cyan) (P < 0.01). (a) left parasagittal, (b) coronal, (c) right parasagittal, (d) inferior axial, (e) medio axial, and (f) superior axial sections. Assignments: R = right; L = left; f.h. = fissura horizontalis; f.p.= fissura prima; f.sec. = fissura secunda; f.s.p.= fissura superior posterior. The outline of the activation is mainly confined to the cerebellar cortex, and the course of the foliae and larger fissures (a, b, c). Note the poor overlap of right and left arm (b), and of the adjacent arm and lip areas (a, c, e). The primary fissure separates the arm area in lobulus HVb from the lip area in HVI (e). In the upper cerebellum, two separate arm areas are

lateral regions of the hemisphere. A second AV (612 mm<sup>3</sup>) was found in medial HVIII, following the course of two folia for approximately 15 mm.

At the lower threshold both AVs merged into one another, as now the whole right hemivermis from V to VIII was included. This large AV nearly filled the right

#### Figure 3.

Group activation maps during movements of the arm (right hand = red; left hand = green, upper row) and face (lips = blue, middle row; tongue = yellow, lower row) at two different correlation levels (right column P < 0.01, left column P < 0.05) in sagittal, coronal, and axial projections. The color intensity scales the correlation coefficient from threshold to the maximum. The axes are scaled in mm. Assignments: R = right; L = left.

found, one vermal in Va (b, e) and a second HVb in the intermediate hemisphere (a, c, e). The intermediate arms and lips areas do not reach the lateral zone of the hemisphere, and spare the medial aspect of the intermediate hemisphere (e). Only the rostral border of the arm reaches the fissura intraculminaris II, thus sparing HVa (a, c, f). Note also, that, while the activation in the upper cerebellum reaches cerebellar surface, the activation in the lower cerebellum is restricted to the depth of the fissures (a, c, d). There is only little ipsilateral activation during right (c) and left (f) foot movement in HIV. Neither within the white matter, nor in the cerebellar nuclei, was no activation found.

spino-cerebellum. The caudal borders of the upper cluster moved across the primary fissure and were now located within VIf–a/HVIf–a. Also, a small contralateral AV was now found laterally in the left-hand region. Furthermore, neocerebellar AVs emerged bilaterally in HVIIA cr.I.

# Left hand

The activation-pattern of the left hand mirrored that of the right hand (Figs. 3, 4). This symmetry of the AVs for the left hand (upper: 3,735 mm<sup>3</sup>; lower: 383 mm<sup>3</sup>) was found with respect to location, shape, and volume as well as the position of the MCs (Table II). The upper AV was, again, composed of



Figure 5.

Intralimb movements of the right arm. Coronal and axial maximum-intensity-projections of the correlation coefficients. The axes are scaled in mm. R =right. Group results (P < 0.01) of movements of the right elbow (brown), wrist (yellow), thumb (green), index (cyan), ring (blue), and little finger (violet). Note

that both the wrist and the thumb have local maxima in the vermis and the hemisphere, which are connected by a thin band—at a lower degree of correlation—similar to the pattern of the hand (Fig. 4).

two clusters, one in Vb-f, connected over a thin band in HVb-c with the second one in HVb-f and HVId. In contrast to the right hand, the vermal cluster slightly crossed the midline. The second, lateral cluster again respected the fissura prima and intraculminaris II as caudal and rostral borders, and the medial and lateral borders were 15 mm and 30 mm apart from the midline. The lower AV was located in HVIII, at the same cranio-caudal level as the corresponding AV for the right hand. A third small AV was found contralaterally in HVd-e, 25 mm apart from the midline, in the same region activated by the right hand. At the lower correlation level (P < 0.05) the AVs expanded and the upper AV now included vermal VI-VIII. And again a neocerebellar AV was now present in contralateral HVIIA cr.I.

### **Right foot**

Movement of the right foot was associated with nearly exclusively ipsilateral activation (Table II; Fig. 4). The largest AV (138 mm<sup>3</sup>) was found in HIV, running with the course of the foliae from about 10 mm medially from the midline to the most lateral aspect of HIV. A second AV (37 mm<sup>3</sup>) was present in medial HIX, ipsilaterally, following the course of the foliae. There were several smaller activation spots, one in ipsilateral HVc, two bilaterally in HVI (both about 30 mm from the midline), and a last one in contralateral HVI, near the primary fissure, several mm alongside the paravermal groove.

# Left foot

One AV (114 mm<sup>3</sup>) in ipsilateral HIV was found, reaching from the paravermal groove to the lateral border of the hemisphere, which followed the course of the foliae (see Fig. 4).

### **Right elbow**

Two ipsilateral AVs were found in the vermis (Fig. 5). A first large AV (717 mm<sup>3</sup>) was located in Va–f with a MC in Vf. It extended slightly lateral into the hemisphere, and caudally crossed the primary fissure to VId–e. The second, smaller volume (24 mm<sup>3</sup>) was located in HVb–c, 20 mm apart from the midline.

# **Right wrist**

A large ipsilateral AV (2,799 mm<sup>3</sup>) extended from Vc–f to HVB (Fig. 5). The lateral border was about 35 mm from the midline. Paravermal HVBd–f were spared, and in the more lateral aspect, the primary fissure was slightly transversed caudally. The AV exhibited three MCs (the highest in HVb–c close at the lateral border). These constituted a crest running from lateral to medial. A second, smaller ipsilateral AV (322 mm<sup>3</sup>) was housed in the medial part of HVIII.

# Right thumb

A large AV (2,117 mm<sup>3</sup>) was located ipsilateral in HVb–f, and crossed the primary fissure to HVI (Fig. 5). In its lateral extension, it reached from V to HVB. It spared the medial aspect of the lamellae d–f in the hemisphere, and extended in its most lateral aspect into lamellae HVId–f. Its lateral border was about 35 mm apart from the midline. A second AV (155 mm<sup>3</sup>) was found in the medial aspect of HVIII.

# Right index finger

The right index finger exhibited one large AV (582 mm<sup>3</sup>) ipsilateral in HVb–d with its medial border 15 mm apart from the midline and a second smaller AV (10 mm<sup>3</sup>) ipsilateral in Vf (Fig. 5).

# Right middle finger

One small AV (24 mm<sup>3</sup>) was found ipsilateral in HVc–d with its medial border 17 mm apart from the midline.

# Right little finger

For the fifth finger, one AV (128 mm<sup>3</sup>) was found ipsilateral in HVc-d with its medial border 20 mm apart form the midline.

# Intralimb arrangement

The AVs exhibited during movements in the right elbow, wrist, and finger were almost completely within the representation of the right hand (Fig. 6). The elbow AV was essentially restricted to the vermis. Wrist and thumb AVs overlapped considerably. The wrist AV consisted of a broad medio-laterally arranged activation with a crest of local maxima running from Ve–f to intermediate HVb–c, lying rostrally to the MCs of fingers I, II, III, and V. The finger AVs showed markedly different volumes: thumb: 2,117 mm<sup>3</sup>; index finger: 582 mm<sup>3</sup>; middle finger: 24 mm<sup>3</sup>; little finger: 128 mm<sup>3</sup> (Table III). The thumb AV covered those of all other fingers. The index finger AV covered fingers III and V. The medial borders of the finger clusters were somatotopically arranged, with the AV of the thumb lying most medially and, laterally, followed by fingers II, III, and V. The corresponding MCs were located along the foliae HVc–d, at the dorsal border of the hand and were arranged such that the index finger was most medial, followed by fingers III, II, and, most laterally, finger V.

# DISCUSSION

# Individual versus group results

The individual maps for hand and lip movement appear quite variable and reveal a rather widespread pattern with considerable differences in location and extent for each of the movements (Fig. 2). The most constant features are the activations of the ipsilateral intermediate upper cerebellum while making fists, and a bilateral activation for movements of the lips caudally adjacent to the hand area. An ordered relationship among different activations in the cerebellum is hardly visible, however, and mostly concealed by additional continuous or fragmented bands of activations spread more or less over the whole cerebellar cortex. The individual activation maps observed in prior fMRI studies, however, exhibit similar features [Ellerman et al., 1994; Britsch et al., 1996; Nitschke et al., 1996; Sakai et al., 1998].

Inasmuch as force, extent, and speed of motion, as well as accompanying stabilization and alignment procedures, depend to large degree upon individual performance, one has to expect variability among individual cerebellar activations-even for defined motions, as a rule. Nevertheless, consistently observed particular activations of areas over subjects would suggest those regions to be essentially involved in a given movement. Each of these movements could be performed with high degree of reproducibility in a relaxed position with immobilized head and shoulder. In this respect we are in line with the vast majority of functional motor studies in humans, which have relied on automatic or semiautomatic motor tasks with defined temporal pacing to monitor activation of particular movements under natural conditions (Table I). For such conditions it has to be assumed that all sensory inputs from mossy fibers, climbing fibers, and cortico-ponto-cerebellar pathways will project simul• Grodd et al. •





Intralimb topography. (a) Right hemicerebellum with hand clusters from Figure 3a. (b) The biggest clusters of the elbow, wrist, and fingers, color-coded, outlined, and superimposed on the gray-scaled hand area. Hand, wrist, and thumb movement exhibit activations in nearly the same areas in V and HV. Wrist and thumb movements are further correlated with activations in HVIII. Both areas are localized within the hand area. Movement in the elbow

taneously, and may cause particular activation in areas where they interact.

### **Cranio-caudal alignment**

By outlining a somatopic arrangement, group activations show two major alignments: one in the craniocaudal and a second in the medio-lateral direction. The cranio-caudal alignment reveals an upside-down order of body parts from HIV to HVI in the upper cerebellum. Movements of the feet fall into HIV.

yields activations in the vermal zone of the hand area only. (c) Blowup defined by the inserts in (a). The highest activated  $10 \text{ mm}^3$  of the elbow, wrist, and fingers are shown, superimposed on the hand area again. The fingers are aligned along the dorsal border of the hand area in HVd, near the primary fissure. The wrist maximum is located more ventrally.

Movements of the hands, in the right elbow joint, in the right wrist and of all right fingers exhibit AVs in V/HVB, thus defining a common area for arm movements. Movements of the lips and tongue fell into HVIA, thus defining a face area. Furthermore, these activations seem to respect anatomical structures. This is best recognized for the hands, where the AVs are confined to the course of the primary fissure (Fig. 3). A second cranio-caudal alignment is found in the lower cerebellum, extending from HVIII to HIX. The foot is represented in HIX. Arm as well as face movements fell into HVIII, and both were confined to the depth of the fissures. Here, however, arm and face representations are juxtaposed and thus a somatotopic arrangement is less obvious.

### Human imaging

In PET studies, an increase in regional cerebral blood flow was found in the ipsilateral superior cerebellum during finger movement and tactile stimulation (Table I). Movements of the hand, and in the wrist, elbow, and shoulder joints caused similar activations in the anterior lobe [Fox et al., 1985; Colebatch et al., 1991; Grafton et al., 1993]. fMRI studies could assign the activation for movements in finger, wrist, and hand joints more precisely to intermediate HIV, HV, vermal I-V, HVI, and HVIII [Britsch et al., 1996; Nitschke et al., 1996; Allen et al., 1997; Desmond et al., 1997; Flament et al., 1996]. Lip and tongue movements activated within HVI [Nitschke et al., 1996; Desmond et al., 1997]. Foot movements were associated with activation in HII to HIV [Britsch et al., 1996; Nitschke et al., 1996]. The only different allocation-with one large activation extending from HIV to HIX—was described by Jüeptner et al. [1997] for elbow movements in a PET study using low resolution. Colebatch et al. [1991] reported cerebellar activation for movements in the shoulder but not for finger and hand movements. In the inferior cerebellum, the foot representation was found in HIX [Britsch et al., 1996].

### Animal electrophysiology

The projection of the group results on a single cerebellar surface (Fig. 7) shows that the topographical relation in the upper as well as in the lower cerebellum is in a close correspondence with the cranio-caudal topography for face, arm, and foot, reported by Snider and Eldred [1951] in cats and monkeys. Since then, however, more refined micromapping procedures at a 50 µm level of resolution in opossums, rats, and cats (Fig. 8) revealed, for a variety of sensory qualities, that body parts are not represented continuously [Shambes et al., 1978; Welker, 1987]. Instead, they are broken into smaller, discontinuous patches, where (i) adjacent patches receive inputs from nonadjacent body parts and (ii) each body part is represented in several disseminated patches. This somatotopic patchy-mosaic feature was referred to as fractured somatotopy.

Parallel to the findings of the Wisconsin group, a second arrangement was described by Voogd [1967], Oscarsson [1996] and Ekerof et al. [1991]. His group found a sagittal organization for the climbing fibers,

with at least eight medio-laterally arranged zones (Fig. 8b). In both the fractured maps and the sagittal zones, a strict somatotopic arrangement was present only within patches or zones. A larger scale cranio-caudal somatotopy, however, was not revealed. Kassel et al. [1984], discussing the results of patchy mosaic, sagittal zonation, and earlier findings concluded that the findings of Snider and Eldred [1951] could not simply result from spatial averaging of fractured patches (Fig. 8).

The same discrepancy exists between micromapping and our findings. In fMRI, lip-pursing led to HVI activation but spared HVII, whereas, in contrast, Welker [1987] found widespread perioral sensory mossy-fiber input in HVI and HVII (Fig. 8c). For the movements of the hand, it is important that both activations in HV and HVIII are exclusively targeted by cortico-ponto-cerebellar projections from Brodmann's areas 4, 5, and 6 [Brodal, 1980; Middelton and Strick, 1997]. Our examinations of movements were performed under conditions that might be more closely related to the conditions of Snider and Eldred [1951], who achieved an orderly topography by mapping both cerebellar inputs—the sensory periphery and the cerebral cortex.

### **Medio-lateral alignment**

The fMRI activation for right- or left-sided movements was predominantly ipsilateral and respected the midline. This was especially evident in the representation of the hands in the upper cerebellum (Figs. 3a–b, 4). If bilateral structures were involved in motion, such as those of the lips and the tongue, hemispheric activation was bilateral and symmetric, with a lower activation of the vermis in between. Hand movement at the lower threshold (P < 0.05) showed a continuous ipsilateral AV in V–VIII, HV, and HVIII, which was restricted to the medial part of the cerebellum and did not involve the lateral part (Fig. 3b). The shape of the hand area (Fig. 3b) resembled the shape of the spino-cerebellum in the classical paper of Dow and Andersen [1942].

A more refined medio-lateral functional segregation was detectable within the upper cerebellum. There, two different clusters were found in the hand area. The first extends from 0 to 5 mm, and the second from 10 to 30 mm lateral to the midline (Figs. 3a and 4e). Both clusters were separated and laterally confined by functionally silent regions, thus forming a medio-lateral zonation. This medio-lateral alignment was refined for movements of parts of the right arm: movement in the elbow joint leads to a predominant





b)









f)

Figure 7.

activation within the vermal part of the hand area, while movements of finger II, III, and V cause activation within the lateral hand area. The MCs for thumb and wrist movements were found lateral in the hand area, but both of the AVs were nearly identical with the hand AV (Fig. 6). As the vermis is designated to posture control [Dichgans and Diener, 1985], it seems reasonable that complex joint movements of the wrist and thumb, or composed movements such as fist clenching, cause additional activation in the vermis.

### Human imaging

Early PET results [Fox et al., 1985] identified mediolaterally oriented ellipses of activation associated with hand and arm movements. Ipsilateral fragmented medio-laterally and sagittally oriented bands of activation have been reported by several groups [Ellerman et al., 1994; Britsch et al., 1996; Nitschke et al., 1996; Sakai et al., 1998]. Colebatch et al. [1991] described vermal activation during shoulder movements. Desmond et al. [1997] reported on group results for finger tapping with a bilocal activation in the vermis and the hemispheres separated by a functionally silent region. In single-subject studies, however, it has been questioned whether an intralimb somatotopy exists [Grafton et al., 1993; Nitschke et al., 1996]. In contrast to most studies on cortical organization in the telencephalon, an averaging over subjects for a probabilistic determination of functional activation has rarely been performed for the cerebellum.

### Animal electrophysiology

The medio-lateral arrangement of activation areas observed in the present study is in accordance with the findings of Snider and Eldred [1951]. Only the alignment of the fingers is different. Whereas Snider

### Figure 7.

Functional somatotopy of the cerebellum. Display of a single cerebellar surface with superimposed color-coded fMRI activation volumes with oblique cranio-caudal (**a**) and dorsal view (**b**) of the cerebellar surface. (**c**) Display of the cerebellar homunculi as represented by Snider and Eldred (1951). (**d**) Blowup of the right hand area from (**a**) with superimposed activation maxima for elbow, wrist, and finger movement. (**e**) Oblique caudo-cranial view on the cerebellar surface. (**f**) Schematic impression of right arm finger positions shown in (**d**). Assignments: E = right elbow; W = right wrist; I, II, III, V = fingers I, II, III, V. Colors: blue = feet; green = left hand; red = right hand; yellow = tongue; dark blue = lips; light brown = elbow; gray-green = wrist; white circles = fingers.

and Eldred found them cranio-caudally aligned, we see them oriented along the primary fissure (Fig. 6b). Our results are furthermore in accordance with those of Voogd [1967], who found various sagittal strips running through the entire extent of the cerebellum. The intermediate zone within lobule IV, V, and VI, is subdivided into the zones C1, C2, and C3, from medially to laterally [Voogd, 1967; Oscarsson, 1976; Ekerot et al., 1991]. The zones targeted by the pathways of the forelimbs are C1 and C3, sparing C2 [Ekerot et al., 1991]. The lateral cluster of hands and lips in our results seem to define a comparable zonation of the intermediate cerebellum.

Furthermore, Ekerot et al. [1991] describe a detailed topography of the forelimb of the cat within C3, where the receptive fields for the digits are represented near the primary fissure (Fig. 8b). Such an alignment of MC for fingers along the primary fissure emphasizes a specific role for intermediate HVd in finger movement control. Patchy mosaic studies, on the other hand, failed to detect a medio-lateral differentiation. These observations remain in contrast to our results. Middelton and Strick [1997], however, followed the connections between the arm area of the motor cortex and the cerebellar cortex in monkeys by using virus tracking, and identified the cerebellar arm-areas in V, HV, and HVIII (Fig. 8d). These results agree with ours in the cranio-caudal arrangement, and they also detected a sparsely stained paravermal area between V and the more lateral zone in HV.

### **Methodological considerations**

### Resolution in space

fMRI as a cross section imaging modality is, in contrast to electrophysiology, not restricted to the cerebellar surface, but instead can depict the whole organ with all major cortical foldings. The fMRI sequence used in this study provided a voxel size of  $3 \times 3 \times 4$  mm. As the individual data sets with different positions and dimensions were transformed and linked together for group analysis, the functional data were reinterpolated to a voxel size of  $1 \times 1 \times 1$  mm<sup>3</sup>. Accordingly, all group data (position and outline of AVs and MCs) could be determined and depicted in a scale of millimeters (Fig. 4a–c).

With respect to spatial resolution, electrophysiological micromapping, which is usually executed in the submillimeter range, is superior to fMRI. However, the patch dimensions reach from  $0.5 \times 0.5 \text{ mm}^2$  for facial, paw, and forelimb [Shambes et al., 1978, Fig. 5; Welker, 1987, Fig. 6; Bower and Woolston, 1983, Fig. 6]





Maps of cerebellar functions from different studies superimposed on a cerebellar matrix scheme of an unfolded hemicerebellum with the midsagittal border on the left side, cranial parts on the top. The rows are labeled according to Larsell and Jansen [1971] and the columns are labeled according to Voogd and Glickstein [1998]. Larger fissures are labeled. Foliae, which are buried in the depth of the fissures, are shaded gray. The colors indicate different body parts as defined on the bottom. (a) Results of Snider and Eldred [1951] of spino- and cerebro-ponto-cerebellar projections as

to about 2 × 1 mm<sup>2</sup> [Kassel et al., 1984, Fig 4; Welker, 1987, Fig. 4, 5, 6, 7; Bower, 1997, Fig. 1]. Ekerot and Larson [1980, Fig. 5] showed a forelimb area of  $\approx 5 \times$ 6 mm<sup>2</sup>, which is subdivided into C<sub>3</sub> ( $\approx 2.5 \times 6 \text{ mm}^2$ ), the medial part of C<sub>1</sub> ( $\approx 1 \times 5 \text{ mm}^2$ ) and D<sub>2</sub> ( $\approx 0.5 \times$ 2 mm<sup>2</sup>). Rarely, even larger continuous areas are described reaching 1 × 20 mm<sup>2</sup> for the dorsal forepaw, wrist, forearm [Rushmer et al., 1980], or 3 × 10 mm<sup>2</sup> for hand and fingers [Robertson and Laxer, 1981]. These patches often continue into the depth of the fissures and must therefore be larger than that depicted because of intense cortical folding [Bower, 1997].

Furthermore, all these electrophysiological results were derived from small mammals with small cer-

found in the monkey and hypothesized for man. (b) Results of Oscarsson [1976, Fig. 1] and Ekerot et al. [1991, Fig. 5] of spinoolivo-cerebellar projections in rat and cat. (c) Results of Kassel et al. [1984, Fig. 6] and Welker [1987, Fig. 5, 6] of spinocerebellar projections in oppossum, rat, and cat. (d) Results of Middelton and Strick [1997, Fig. 4] of cerebro-ponto-cerebellar projections in monkey. (e) Present results of presumably spino-, spino-olivo- and cerebro-ponto-cerebellar projections in man.

ebella. The estimated surfaces range from  $\approx 200 \text{ mm}^2$  for the mouse to  $\approx 4,300 \text{ mm}^2$  for cat, and to  $\approx 8,000 \text{ mm}^2$  for the macaque. In contrast, the human cerebellum possesses a considerably larger surface of more than 110,000 mm<sup>2</sup>, mainly because of an increase in size but also an increase in the number of foldings [Sultan and Braitenberg, 1993]. These exceptional dimensions of the human cerebellum itself allow for speculations with respect to the number and extent of functional patches: If one only assumes a constant cortical thickness of 1 mm [Duvernoy, 1995] and an isometric relation for mammals and man, then the increase in patch volume should at least be more than tenfold, or more than a twofold in a single dimension. Such patches should then be

large enough to be detected by fMRI. The same holds true for the sagittal zones, which should reach a medio-lateral extent of about 7 mm. Seemingly, some of our individual activation spots approach the dimensions of larger patches and are likely to represent the spatial and temporal integration of hemodynamic responses accompanying the electrophysiological events in animals.

# Resolution in time

Electrophysiology provides an unsurpassed temporal resolution in the millisecond range. Even though the functional relationship of the BOLD signal with the underlying neuronal activity is still a matter of debate, fMRI only depicts hemodynamic events, where a single response is dispersed for at least 5–10 sec [Janz et al., 1997]. Beyond that, our experiments were performed in a block design so that the hemodynamic response for each repetitively performed task was summarized over six consecutive measurements. Our fMRI method therefore integrates the regional vascular response over a period of 60 sec and averages activation from up to 60 movement repetitions. Such a sampling interval sums up sensory information from repetitively changing proprio- and exteroceptive inputs as wells as accompanying cortical commands. Therefore a direct comparison of fMRI with electrophysiological events has to be handled with care.

### Sensorimotor topography

The somatotopic representation in cortical sensorimotor areas is well established. However, a closer view of the somatotopic representations of the motor system reveals that body-part assignment also depends on the degree of resolution. Even the famous homunculoid maps of the motor cortex of Woolsey [1952] are only approximations of the original data, as the latter were far too complex to be precisely depicted in final drawings. The same holds true for the somatotopic assignments of Penfield and coworkers [Penfield and Boldrey, 1937], who also found a disseminated or "patchy distribution" for the elicitation of certain motor and speech functions.

For the upper cerebellum, we are convinced that the cranio-caudal and medio-lateral alignment sums up to an upside-down somatotopy. Whereas a good differentiation within the face area (lips and tongue) is not achievable, a clear separation exists within the upper limb. Within the hand area, the arrangement of the MCs not only revealed a differentiation of proximal and distal joints, but within the lateral hand area, a

strip along the primary fissure is found where the fingers are aligned (Fig. 6b).

In addition, the AVs decreased in size from wrist over thumb to finger V by more than twenty fold (2,799, 2,117, and 128 mm<sup>3</sup>; see Table III). Such difference in representation size for different body parts is also well known for sensorimotor areas in the telencephalon. This variation can be explained by the very different demands on the sensory input for different movements. Complex joints like the wrist should recruit more proprioceptive information from the muscles, tendons, fascias, and neighboring muscles for synchronous adjustment than the simple joints of the middle or little finger. The different AVs overlap each other, however (Fig. 6a). Wrist and thumb are nearly identical and include the complete area of the second finger, while the latter includes areas of the third and fifth finger. For such an arrangement within a hand area, one could argue again, that thumb tapping requires more stabilization and comovements of other fingers then tapping of the fifth finger.

### Motor and cognitive regions

The variety of sources that contribute to cerebellar activation can be divided into those of central and of peripheral origin, with the vast majority of projections arriving in the cerebellar cortex, having originated from the telencephalon via various cortico-pontine projections. These afferences provide about 20 million fibers in contrast to about 1 million fibers arising from the body's periphery [Rothwell, 1994]. This intense central influence may explain the growing evidence of extensive cerebellar involvement in cognitive processes [Schmahmann, 1997; Flament et al., 1996; Allen et al., 1997; Sakai et al., 1998]. Gao et al. validating the concepts of Bowers stated that "the lateral cerebellum is not activated by the control of movement per se, but is strongly engaged during the acquisition and discrimination of sensory information... and cognitive performances specifically because of the requirement to process sensory data" [Gao et al., 1996]. This agrees well with our study, in which the activations for rhythmic movements of face and arm were limited to the medial cerebellum. All activation in this medial compartment add up to  $\approx 15,000 \text{ mm}^3$  and cover only 15-20 % of the whole cerebellar cortex [Braitenberg and Atwood, 1958], given a cortical thickness of 1 mm [Duvernoy, 1995].

### CONCLUSIONS

Until very recently, experimental animal studies have been our primary guides to understanding the

functional organization of the cerebellum. The results presented here demonstrate that fMRI is well suited to depict similar functional features in the human cerebellum, but that an adapted normalization procedure is mandatory to reveal an interindividual constant topology of cortical activation.

According to the results presented here:

(a) There exists a medial compartment of the cerebellum located in V, HV, VI, HVI, and HVIII, which comprises a volume of about 15,000 mm<sup>3</sup>. This compartment is mainly concerned with the execution and control of voluntary movements of arm and face.

(b) This compartment is subdivided along its transverse axis into at least four functional sagittal zones: a vermal, paravermal, intermedio-lateral, and a lateral zone. The vermal and intermedio-lateral zone are active during repetitive movements of the distal arm and of the face.

(c) With respect to feet, arms, and face, a somatotopically organized body representation exists within the upper human cerebellum: an upside-down homunculus. Within the arm area, the movements in the elbow are represented medially, whereas movements in the wrist and the fingers are represented in the intermedio-lateral zone. There is additional evidence that, within this intermedio-lateral zone, wrist, and finger areas can be distinguished and that the intermedio-lateral HVd may therefore play a special role for finger movements.

(d) A second body-representation seems to exist in the lower cerebellum in HVIII-HIX. This may be somatotopically arranged along cranio-caudal and medio-lateral axes.

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